AMENDMENTS TO THE CLAIMS

Applicants respectfully request that the following amendments be entered and that it be done without prejudice, without admission, without intentional surrender of subject matter, and without any intention of creating any estoppel as to equivalents. The following listing of the claims will replace all prior versions and all prior listings of the claims in the present application:

1. (Currently amended) A method of identifying a marker useful for detecting diabetes, said method comprising:

a) using an oligonucleotide of predetermined sequence, detecting a presence in RNA of blood samples which have not been fractionated into cell types from subjects having diabetes, of RNA encoded by a gene, said gene expressed in blood and in a non-blood tissue of a subject not having diabetes, said oligonucleotide being specific only for RNA encoded by said gene in said samples, and/or for cDNA complementary only to ~~said~~ RNA,‑ encoded by said gene in said samples,‑;

b) quantifying a level of ~~said~~ RNA encoded by said gene in said samples; and

c) determining a difference between said ~~quantified~~ level and a quantified level of ~~a control~~ RNA encoded by said gene in RNA of blood samples which have not been fractionated into cell types from control subjects, ~~said control~~ RNA encoded by said gene having been detected in said samples from said control subjects, thereby identifying said gene as being a marker useful for detecting diabetes.

2. (Currently amended) A method of identifying two or more markers useful for

detecting diabetes, said method comprising:

for each gene of a collection of two or more genes, said gene being expressed in blood

and in a non-blood tissue of a subject not having diabetes;

a) using an oligonucleotide of predetermined sequence, detecting a presence in

RNA of blood samples which have not been fractionated into cell types from

subjects having diabetes, of RNA encoded by said gene, said oligonucleotide

being specific only for RNA encoded by said gene in said samples, and/or for

cDNA complementary only to said RNA, encoded by said gene in said samples,

said gene being expressed in blood and in a non-blood tissue of a subject not

having diabetes;

b) quantifying a level of said RNA encoded by said gene in said samples; and

c) determining a difference between said level and a quantified level of RNA

encoded by said gene in RNA of blood samples which have not been fractionated

into cell types from control subjects, RNA encoded by said gene having been

detected in said samples from said control subjects,

thereby identifying said two or more genes as two or more markers useful in for detecting

diabetes.

3.   (Currently amended) A method of identifying a marker useful for detecting

diabetes, said method comprising:

a) producing amplification products from RNA of blood samples which have not

been fractionated into cell types, from subjects having diabetes, using primers

specific only for RNA encoded by a gene in said samples, and/or for cDNA

complementary <u>only</u> to ~~said~~ RNA,~~,~~ encoded by a <u>said</u> gene in said samples, said

gene being expressed in blood and in a non-blood tissue of a subject not having

diabetes;

b) quantifying a level of said amplification products; and

c) determining a difference between said ~~quantified~~ level ~~of said amplification~~

~~products~~ and a quantified level of amplification products produced using primers

specific ~~only~~ for RNA <u>encoded by said gene</u>, and/or <u>for</u> cDNA complementary to

~~said~~ RNA, encoded by said gene, from ~~control RNA, in~~ RNA of blood samples

which have not been fractionated into cell types~~, said control RNA having been~~

~~detected in said samples~~ from ~~said~~ control subjects,

thereby identifying said gene as ~~being~~ a marker useful for detecting diabetes.

4.   (Currently amended) A method of identifying two or more markers useful for

detecting diabetes, said method comprising:

for each gene of a collection of two or more genes<u>, wherein said gene is expressed in</u>

<u>blood and in a non-blood tissue of a subject not having diabetes</u>;

a) producing amplification products from RNA of blood samples which have not

been fractionated into cell types from subjects having diabetes, using primers

specific only for RNA <u>encoded by said gene in said samples</u>, and/or <u>for</u> cDNA

complementary <u>only</u> to ~~said~~ RNA,~~,~~ encoded by said gene ~~of said subjects~~ <u>in said</u>

<u>samples</u>~~, wherein said gene is expressed in blood and in a non-blood tissue of a~~

~~subject not having diabetes~~;

b) quantifying a level of said amplification products; and

c) ~~D~~determining a difference between said ~~quantified~~ level ~~of said amplification products~~ and a quantified level of amplification products produced, using primers specific ~~only~~ for RNA <u>encoded by said gene</u>, and/or <u>for</u> cDNA complementary to ~~said~~ RNA, encoded by said gene, from ~~control RNA in~~ RNA of blood samples which have not been fractionated into cell types, from control subjects, ~~said control RNA having been detected in said samples from said control subjects~~, thereby identifying ~~said collection of~~ said two or more genes as two or more markers useful for detecting diabetes.

5. (Currently amended) The method of any one of claims 1-4, wherein ~~each of said one or more markers corresponds to~~ <u>said gene is</u> a non immune response ~~genes~~ <u>gene</u>.

6. (Canceled)

7. (Currently amended) The method of any one of claims 1-4, wherein ~~each of said one or more markers corresponds to a~~ <u>said</u> gene <u>is</u> expressed by non-lymphoid tissue.

8. (Currently amended) The method of any one of claims 1-4, wherein said diabetes is ~~either~~ <u>selected from the group consisting of</u> symptomatic <u>diabetes</u> ~~or~~ <u>and</u> asymptomatic <u>diabetes</u>.

9.　　(Previously presented)　The method of any one of claims 1-4, wherein said diabetes is type II diabetes.

10.　　(Currently amended)　The method of any one of claims 1-4, wherein said ~~one or more markers identifies one or more genes~~ gene is selected from the group of genes listed in Table 3G.

11.　　(Canceled)

12.　　(Currently amended)　A method of detecting a difference in expression of a gene in a human test subject suspected of having diabetes ~~as compared with~~ relative to healthy human control subjects, said method comprising:

　　　a) using an oligonucleotide of predetermined sequence, detecting in RNA of a

　　　blood sample from said test subject which has not been fractionated into cell

　　　types, RNA encoded by said gene~~in said sample~~, wherein said gene is expressed

　　　in blood and in a non-blood tissue in a subject who is not said test subject, said

　　　oligonucleotide being specific only for RNA encoded by said gene in said

　　　sample, and/or for cDNA complementary only to ~~said~~ RNA~~,~~ encoded by said

　　　gene in said sample;

　　　b) quantifying a level of ~~said~~ RNA encoded by said gene in said sample; and

　　　c) determining a statistically significant difference where p< 0.05, between said

　　　level and a quantified level of ~~control~~ RNA encoded by said gene in RNA of

blood samples which have not been fractionated into cell types from said control

subjects, <u>RNA encoded by said gene having been detected in said samples</u>

~~wherein said difference is indicative of diabetes in said test subject~~,

thereby detecting a difference in expression of said gene in said human test subject vs. said

human control subjects.

13.   (Currently amended) A method of detecting a difference in expression of ~~each~~ <u>a</u>

<u>collection</u> of two or more genes ~~of~~ <u>in</u> <u>a</u> human test subject<u>s</u> <u>suspected of having diabetes</u> ~~vs.~~

<u>relative to</u> <u>healthy</u> human control subjects;

<u>for each gene of said collection of two or more genes, wherein said gene is expressed in</u>

<u>blood and in a non-blood tissue in a subject who is not said test subject,</u>

a) using an oligonucleotide of predetermined sequence, detecting in RNA of a

blood sample from said test subject which has not been fractionated into cell

types, RNA encoded by said gene~~in said sample, wherein said gene is expressed~~

~~in blood and in a non-blood tissue in a subject who is not said test subject,~~ said

oligonucleotide being specific only for RNA <u>encoded by said gene in said sample,</u>

<u>and/</u>or <u>for</u> cDNA complementary <u>only</u> to said RNA~~,~~ encoded by said gene <u>in said</u>

<u>sample</u>; ~~and~~

b) quantifying a level of said amplification product; and

c) determining a <u>statistically significant</u> difference <u>where p< 0.05,</u> between said

level and a quantified level of control RNA encoded by said gene in RNA of

blood samples which have not been fractionated into cell types from said one or

more control subjects, ~~said control~~ RNA <u>encoded by said gene</u> having been detected in said samples ~~for~~<u>from</u> said control subjects; ~~wherein said difference for each said gene is indicative of diabetes in said test subject,~~

thereby detecting a difference in expression of each <u>of</u> said gene in said collection of two or more genes in blood of said human test subject~~s~~ vs. said human control subjects.

14. (Currently amended) A method of detecting a difference in expression of a gene ~~of~~<u>in</u> a human test subject <u>suspected of having diabetes</u> ~~vs.~~ <u>relative to</u> <u>healthy</u> human control subjects, said method comprising:

a) producing amplification products from RNA of a blood sample from said test subject which has not been fractionated into cell types, using primers specific only for RNA <u>encoded by said gene in said sample,</u> and/or <u>for</u> cDNA complementary <u>only</u> to ~~said~~ RNA~~,~~ encoded by said gene <u>in said sample</u>, wherein said gene is expressed in blood and in a non-blood tissue of a subject who is not said test subject;

b) quantifying a level of said amplification product; and

c) determining a <u>statistically significant</u> difference <u>wherein p< 0.05,</u> between said ~~quantified~~ level ~~of said amplification products~~ and a quantified level of amplification products produced using primers specific ~~only~~ for RNA <u>encoded by said gene,</u> and/or <u>for</u> cDNA complementary to ~~said~~ RNA~~,~~ encoded by said gene, ~~applied to control~~ <u>from</u> RNA of blood samples which have not been fractionated into cell types from said control subjects, ~~wherein detection of said difference for~~

~~said gene is indicative of diabetes in said test subject,~~

thereby detecting a difference in expression of ~~each~~ said gene in said ~~collection of two or more genes in blood of said~~ human test ~~subjects vs.~~ subject relative to said human control subjects.

15.   (Currently amended)   A method of detecting a difference in expression of ~~each~~ a collection of two or more genes ~~of~~in a human test subject suspected of having diabetes ~~vs~~ relative to healthy human control subjects, said method comprising:

for each gene of said collection of two or more genes, wherein said gene is expressed in blood and in a non-blood tissue of a subject who is not said test subject:

a) producing ~~an~~ amplification product_s_ from RNA of a blood sample from said test subject which has not been fractionated into cell types, using primers specific only for RNA encoded by said gene in said sample, and/or for cDNA complementary only to ~~said~~ RNA, encoded by said gene in said sample ~~wherein said gene is expressed in blood and in a non-blood tissue of a subject who is not said test subject~~; ~~and~~

b) quantifying a level of said amplification product_s_~~,~~; and

c) determining a statistically significant difference wherein p< 0.05, between said ~~quantified~~ level ~~of said amplification product~~ and a quantified level of amplification products produced using primers specific ~~only~~ for RNA encoded by said gene, and/or for cDNA complementary to ~~said~~ RNA, encoded by said gene, ~~applied to control~~ from RNA of blood samples which have not been fractionated

into cell types from said control subjects, ~~said control RNA having been detected in said samples from said control subjects, wherein determining a difference for each said gene is indicative of diabetes in said test subject,~~

thereby detecting a difference in expression of ~~each said gene in~~ said collection of two or more genes in ~~blood of~~ said human test subject~~s vs.~~ <u>relative to</u> said human control subjects.

16.   (Canceled)

17.   (Currently amended) The method of any one of claims 12-15, wherein ~~each of~~ said ~~genes~~ <u>gene</u> is selected from the genes listed in Table 3G.

18.   (Canceled)

19.   (Currently amended) The method of any one of claims 12-15, wherein said diabetes is ~~either~~ <u>selected from the group consisting of</u> symptomatic <u>diabetes</u> ~~or~~ <u>and</u> asymptomatic <u>diabetes.</u>

20.   (Previously presented) The method of any one of claims 12-15, wherein said diabetes is type II diabetes.

21.-24.   (Canceled)

25.   (Previously presented) The method of any one of claims 1-4 and 12-15, further comprising the step of isolating RNA from said samples.

26.   (Previously presented) The method of any one of claims 1-2 and 12-15, wherein said steps of determining said levels of RNA encoded b said gene in step (a) and/or step (b) is effected using quantitative RT-PCR (QRT-PCR).

27.   (Canceled)

28.   (Previously presented) The method of any one of claims 3-4 and 14-15, wherein said primers are 15-25 nucleotides in length.

29.   (Canceled)

30.   (Currently amended) The method of any one of claims 1-4 and 12-15, wherein the step of determining said levels of RNA encoded by each of said genes in step (a) and/or step (b) is by e hybridizing a first plurality of isolated nucleic acid molecules that correspond to said genes to an array comprising a second plurality of isolated nucleic acid molecules.

31.   (Original) The method of claim 30, wherein said first plurality of isolated nucleic acid molecules comprises RNA, DNA, cDNA, PCR products or ESTs.

32.   (Original) The method of claim 30, wherein said array comprises a plurality of isolated nucleic acid molecules comprising RNA, DNA, cDNA, PCR products or ESTs.

33.   (Canceled)

34.   (Original) The method of claim 32, wherein said array comprises two or more of the markers of claim 2.

35.   (Original) The method of claim 32, wherein said array comprises two or more of the markers of claim 3.

36.   (Original) The method of claim 32, wherein said array comprises two or more of the markers of claim 4.

37.   (Original) The method of claim 32, wherein said array comprises a plurality of nucleic acid molecules that correspond to genes of the human genome.

38. (Withdrawn) The method of claim 32, wherein said array comprises a plurality of nucleic acid molecules that correspond to two or more sequences of two or more genes selected from the group of genes listed in Table 3G.

39. (Withdrawn) A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 1.

40. (Withdrawn) A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 2.

41. (Withdrawn) A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 3.

42. (Withdrawn) A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 4.

43. (Canceled)

44. (Withdrawn) An array consisting essentially of the plurality of nucleic acid

molecules of claim 39.

45.   (Withdrawn) An array consisting essentially of the plurality of nucleic acid molecules of claim 40.

46.   (Withdrawn) An array consisting essentially of the plurality of nucleic acid molecules of claim 41.

47.   (Withdrawn) An array consisting essentially of the plurality of nucleic acid molecules of claim 42.

48.   (Withdrawn) A kit for diagnosing or prognosing diabetes comprising:

a) two gene-specific priming means designed to produce double stranded DNA complementary to a gene that corresponds to a marker selected from the group consisting of markers of claim 1, claim 2, claim 3, and claim 4; wherein said first priming means contains a sequence which can hybridize to RNA, cDNA or an EST complementary to said gene to create an extension product and said second priming means capable of hybridizing to said extension product;

b) an enzyme with reverse transcriptase activity;

c) an enzyme with thermostable DNA polymerase activity; and

d) a labeling means;

wherein said primers are used to detect the quantitative expression levels of said gene in a

test subject.

49.   (Withdrawn) A kit for monitoring a course of therapeutic treatment of diabetes,

comprising:

a) two gene-specific priming means designed to produce double stranded DNA

complementary to a gene that corresponds to a marker selected from the group consisting

of markers of claim 1, claim 2, claim 3, and claim 4; wherein said first priming means

contains a sequence which can hybridize to RNA, cDNA or an EST complementary to

said gene to create an extension product and said second priming means capable of

hybridizing to said extension product;

b) an enzyme with reverse transcriptase activity;

c) an enzyme with thermostable DNA polymerase activity; and

d) a labeling means;

wherein said primers are used to detect the quantitative expression levels of said gene in a

test subject.

50.   (Withdrawn) A kit for monitoring progression or regression of diabetes,

comprising:

a) two gene-specific priming means designed to produce double stranded DNA

complementary to a gene that corresponds to a marker selected from the group consisting

of markers of claim 1, claim 2, claim 3, and claim 4; wherein said first priming means

contains a sequence which can hybridize to RNA, cDNA or an EST complementary to

said gene to create an extension product and said second priming means capable of

hybridizing to said extension product;

b) an enzyme with reverse transcriptase activity;

c) an enzyme with thermostable DNA polymerase activity; and

d) a labeling means;

wherein said primers are used to detect the quantitative expression levels of said gene in a

test subject.

51.   (Withdrawn) The kit of any one of claims 48 to 50 wherein said gene-specific

priming means identified in step a) is selected from the group of genes listed in Table 3G.

52.   (Withdrawn) A plurality of nucleic acid molecules that identify or correspond to

two or more sequences of two or more genes selected from the group of genes listed in Table 3G.

53.   (Canceled)

54.   (Previously presented) The method of any of claims 1-4 wherein none of said

control subjects have diabetes.

55.   (Previously presented) The method of any of claims 1-4 wherein said control subjects have diabetes at a different stage than said subjects having diabetes.

56-63.   (Canceled)

64.   (Currently amended) A method ~~for detecting an indication~~ of identifying a human test subject as being a candidate for having Type II diabetes~~in a human test subject~~, comprising:

a) ~~Q~~quantifying in RNA of a blood sample from said test subject, a level of RNA encoded by ~~the gene DAZ interacting protein 1 (a~~ DZIP1~~)~~ gene~~in said sample~~; and

b) ~~C~~comparing said ~~quantified~~ level with a quantified level of ~~control~~ RNA encoded by said gene in RNA of blood samples from control subjects, wherein said control subjects are healthy;

wherein ~~said comparison of said quantified level of step (a) with said quantified level of said control RNA~~ step (b) results in a determination of a statistically significant difference wherein p< 0.05 between said level of step (a) and said quantified level, thereby identifying said test subject as a candidate for having Type II diabetes is indicative of diabetes in said human test subject.

65.   (Previously presented) The method of claim 64, wherein said blood sample of step (a) and said blood samples from said control subjects in step (b) have not been fractionated into cell types.

66.   (Canceled)

67.   (Currently amended) The method of claim 64 or claim 65 ~~any of claims 64, 65 and 66~~, wherein said quantifying of said level of said RNA encoded by said gene in step (a) is effected by quantifying said RNA relative to a housekeeping gene.

68.   (Currently amended) The method of claim 64 or claim 65 ~~any of claims 64, 65 and 66~~, wherein said quantifying of said level of said RNA encoded by said gene in step (a) is effected by quantification of cDNA corresponding to said RNA.

69.   (Canceled)

70.   (Canceled)

71. (Currently amended) The method of <u>claim 64 or claim 65</u> ~~any of claims 64, 65 and 66~~, wherein said quantifying of said level of said RNA encoded by said gene in step (a) is determined using quantitative real-time RT-PCR.

72. (Currently amended) The method of <u>claim 64 or claim 65</u> ~~any of claims 64, 65 and 66~~, wherein said quantifying of said level of said RNA encoded by said gene in step (a) is determined using an array.

73. (New) A method of classifying DZIP1 gene expression in a human test subject, said method comprising:

(a) quantifying a level of RNA encoded by a DZIP1 gene in a blood sample from said test subject;

(b) comparing said level of step (a) with a quantified level of RNA encoded by said gene in blood samples from control subjects having Type II diabetes; and

(c) comparing said level of step (a) with a quantified level of RNA encoded by said gene in blood samples from control subjects who are healthy;

wherein a determination from steps (b) and (c) that said level of step (a) is statistically similar to said levels in said samples from said subjects having diabetes and is statistically different, wherein $p < 0.05$, from said level in said samples from said subjects who are healthy, results

in a classification of DZIP1 gene expression in said test subject with that of said subjects

having diabetes, and

wherein a determination from steps (b) and (c) that said level of step (a) is statistically

different from said level in said samples from said subjects having diabetes and is

statistically similar to said level in said samples from said subjects who are healthy, results in

a classification of DZIP1 gene expression in said test subject with that of said subjects who

are healthy.

74.   (New) The method of claim 73, wherein said blood sample of step (a) and each of

said blood samples from said control subjects has not been fractionated into cell types.

75.   (New) The method of claim 73 or claim 74, wherein said quantifying is effected

relative to a housekeeping gene.

76.   (New) The method of claim 73 or claim 74, wherein said quantifying is effected

by quantifying cDNA corresponding to RNA encoded by said gene.

77.   (New) The method of claim 73 or claim 74, wherein said quantifying is effected

using quantitative RT-PCR.

78.   (New) The method of claim 73 or claim 74, wherein said quantifying is effected using an array.